RESPONSE

I. Status of the Claims

Claim 5 was previously cancelled entirely without prejudice and without disclaimer, as being drawn to a non-elected invention. Claims 1-4 are currently amended to better claim the present invention. Claims 1-4 and 6-9 are presently pending.

II. Support for the Claims

Claims 1-4 are currently amended to remove Markush language which is no longer required and therefore to better claim the present invention.

As amended claims 1-4 are fully supported by the specification, sequence listing and claims as originally filed, they do not constitute new matter. Entry is therefore respectfully requested.

II. Rejection of Claims 3 and 8-9 Under 35 U.S.C. § 112

The Action rejects claims 3 and 8-9 under 35 U.S.C. § 112 because the specification, while being enabling for an isolated cDNA molecule encoding SEQ ID NO: 16 (such as SEQ ID NO: 15) or an isolated host cell, does not reasonably provide enablement for every isolated cDNA molecule that hybridizes under stringent conditions to SEQ ID NO: 15 or a non-isolated host cell that comprises a transgenic primate or human in origin or could result from human genetic therapy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The Action's rejects Claim 3 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention,.because the specification, while being enabling for an isolated cDNA molecule encoding SEQ ID NO: 16 (such as SEQ ID NO: 15) does not reasonably provide enablement for every isolated cDNA molecule that hybridizes under stringent conditions to SEQ ID NO: 15. Applicants respectfully traverse this rejection.

35 U.S.C. § 112, first paragraph, requires that the specification contain a written description of the invention. The Federal Circuit in *Vas-Cath Inc. v. Mahurkar* (19 USPQ2d 1111 (Fed. Cir. 1991); "*Vas-Cath*") held that an "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.*" *Vas-Cath*, at 1117, emphasis in original. However, it is important to note that the above finding uses the terms reasonable clarity to those skilled in the art. Further, the Federal Circuit in *In re Gosteli* (10 USPQ2d 1614 (Fed. Cir. 1989); "*Gosteli*") held:

> Although [the applicant] does not have to describe exactly the subject matter claimed, . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.

Gosteli at 1618, emphasis added. Additionally, *Utter v. Hiraga* (6 USPQ2d 1709 (Fed. Cir. 1988); "*Utter*"), held "(a) specification may, within the meaning of 35 U.S.C. § 112 ¶1, contain a written description of a broadly claimed invention without describing all species that claim encompasses" (*Utter*, at 1714). Therefore, all Applicants must do to comply with 35 U.S.C. § 112, first paragraph, is to convey the invention with reasonable clarity to the skilled artisan.

Further, the Federal Circuit has held that an adequate description of a chemical genus "requires a precise definition, such as by structure, formula, chemical name or physical properties" sufficient to distinguish the genus from other materials. *Fiers v. Sugano*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993; "*Fiers*"). *Fiers* goes on to hold that the "application satisfies the written description requirement since it sets forth the . . . nucleotide sequence" (*Fiers* at 1607). In other words, provision of a structure and formula - the nucleotide sequence - renders the application in compliance with 35 U.S.C. § 112, first paragraph.

More recently, the standard for complying with the written description requirement in claims involving chemical materials has been explicitly set forth by the Federal Circuit:

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. *Univ. of*

California v. Eli Lilly and Co., 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Thus, a claim describing a genus of nucleic acids by structure, formula, chemical name or physical properties sufficient to allow one of ordinary skill in the art to distinguish the genus from other materials meets the written description requirement of 35 U.S.C. § 112, first paragraph. As further elaborated by the Federal Circuit in *Univ. of California v. Eli Lilly and Co.*:

> In claims to genetic material ... a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA', without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art cannot, as one can do with a fully described genus, visualize or recognize the identity of members of the genus. (Emphasis added).

Thus, as opposed to the situation set forth in *Univ. of California v. Eli Lilly and Co.* and *Fiers*, the nucleic acid sequences of the present invention are not distinguished on the basis of function, or a method of isolation, but in fact are distinguished by structural features - a chemical formula, *i.e.*, the *sequence itself.*

The Action (page 3-4) rejects Claim 3, because it allegedly does not reasonably provide enablement for every isolated cDNA molecule that hybridizes under stringent conditions to SEQ ID NO: 15. However, Applicants respectfully submit that Claim 3 has two limitations, the first being that molecules which encode the amino acid sequence shown in SEQ ID NO: 16; and the second being hybridization to the nucleotide sequence of SEQ ID NO: 15 or the complement thereof. Applicants submit that the nucleic acid molecules identified by the intersection of both parts of Claim 3, those that encode the amino acid sequence shown in SEQ ID NO: 16; and hybridize to the nucleotide sequence of SEQ ID NO: 15 or the complement thereof, is a finite and well defined group, which those of skill in the art could easily identify and would know how to make and use. Therefore, Applicants respectfully request that the rejection of Claim 3 under 35 U.S.C. § 112, first paragraph, be withdrawn.

The Action also rejects claims 8-9 under 35 U.S.C. § 112, first paragraph, because it alleges that

the specification, while being enabling for an isolated host cell, does not reasonably provide enablement for a non-isolated host cell, as such could comprise a transgenic primate or human in origin or could result from human genetic therapy. The Examiner further alleges that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the claimed invention, a host cell, commensurate in scope with these claims. Applicants disagree and respectfully traverse.

Specifically the Action (at page 4, lines 11-14) states "the claims encompass the cells of a transgenic animal *per se* (because all animals are made up of cells) such as genetically altered primate, including humans (see page 18, lines 6-24 of the instant specification), which would include transgenic humans" and further alleges that the disclosure does not provide adequate written description or any working examples by which genetic engineering or gene therapy could be accomplished. However, the Action then contradicts its interpretation by stating (on page 5, line 1-3) that claims directed at transgenic animals would constitute a separate invention and be subject to further restriction.

If the Examiner believes, as stated, that claims that read on trangenic animals would constitute a separate invention and thus be subject to further restriction, how can he also reasonably then assert that the alleged failure of the specification to support claims to transgenic animals (which is incorrect) be evidence of a failure of the specification to support a claim directed at a host cell? One must conclude that they either are or are not the same invention. If, as the Examiner states, one assumes that these are separate inventions, then the alleged failure of the specification to support one invention (transgenic animals) is irrelevant to a claim directed at another (a host cell). Thus, the rejection appears to have been made in error and Applicants therefore request withdrawnal.

Even if one were to assume, for arguments sake that the present rejection were proper, the Actions position that the absence of "any working examples" is not dispositive, nor particularly relevant, as to the question of enablement, for it has long been established that "there is no statutory requirement for the disclosure of a specific example" (*In re Gay*, 309 F.2d 769, 135 USPQ 311 (CCPA, 1962)). Thus, this argument alone cannot support an allegation that claims 8-9 are not enabled.

The present application is fully enabling for the claimed invention - a host cell. Many host cells are described in the specification as filed and host cells are very well known to those of skill in the art.

Applicants also note that claims directed at a "host cell" have been allowed in hundreds of patents which contain no more disclosure than the present case (see for example U.S. Patent Nos. 6,531,309, 6,586,230, 6,777,221: **Exhibits A-C**, copies of issued U.S. Patents not provided pursuant to current United States Patent and Trademark Office policy). As issued U.S. Patents are presumed to meet all of the requirements for patentability, including enablement under 35 U.S.C. §112, first paragraph. Therefore, Applicants respectfully submit that the present claim directed at a host cell must also logically be enabled and meet the requirements of 35 U.S.C. § 112, first paragraph.

Furthermore even if, again arguendo, one were to address the Examiner's alleged issues regarding gene therapy, Applicants note that not only would claims drawn to humans, transgenic or otherwise, be non-statutory but that the specification clearly excludes humans by stating "non-human primates" on page 18, "NHP gene products can also be expressed in transgenic animals. Animals of any species, including, but not limited to, worms, mice, rats, rabbits, guinea pigs, pigs, micro-pigs, birds, goats, and **non-human primates,** *e.g.*, baboons, monkeys, and chimpanzees may be used to generate NHP transgenic animals (emphasis added)".

In addition, Applicants herein present evidence of the state of the art with regard to making transgenic animals, as of the filing date of the present application (October 17, 2001), which indicate that in fact the specification as filed is enabling for the generation of non-human trangenic animals. Applicants respectfully point out that there are **numerous** examples of transgenic worms (nematodes), mice, rats, rabbits, guinea pigs, pigs, birds (chickens), goats and monkeys, years and sometimes decades prior to the filing date of the present application. However, rather than provide hundreds of citations of transgenic animals that are in the art prior to the filing date of the present application, Applicants respectfully point out that the first report of a transgenic nematode was in 1988 (Spieth *et al.*, *Dev. Biol.* **130**:285-293; copy of abstract provided in **Exhibit D**), the first report of a transgenic mouse was in 1980 (Gordon *et al.*, *Proc. Natl. Acad. Sci. USA* **77**:7380-7384; copy of manuscript provided in **Exhibit E**), the first report of a transgenic rat was in 1990 (Mullins *et al.*, *Nature* **344**:541-544; copy of abstract provided in **Exhibit F**), the first report of a transgenic rabbit was in 1985 (Hammer *et al.*, *Nature* **315**:680-683; copy of abstract provided in **Exhibit G**), a report of the production of human interleukin-2 in the milk of transgenic rabbits was published in 1990 (Bühler *et al.*, *Bio/Technology* **8**:140-143; copy of abstract

provided in **Exhibit H**), the first reports of transgenic guinea pigs were in 2000 (Suzuki *et al.*, *Gene Ther.* **7**:1046-1054, and Yagi *et al.*, *JARO* **1**:315-325; copies of abstracts provided in **Exhibit I**), a report of the production of human growth hormone in the milk of transgenic guinea pigs was also published in 2000 (Hens *et al.*, *Biochim. Biophys. Acta* **1523**:161-171; copy of abstract provided in **Exhibit J**), the first report of a transgenic pig was in 1985 (see **Exhibit G**), a report of the production of a heterologous milk protein in the milk of transgenic pigs was published in 1991 (Wall *et al.*, *Proc. Natl. Acad. Sci. USA* **88**:1696-1700; copy of manuscript provided in **Exhibit K**), the first reports of transgenic chickens were in 1987 (Salter *et al.*, *Virology* **157**:236-240; copy of abstract provided in **Exhibit L**) and 1989 (Bosselman *et al.*, *J. Virol.* **63**:2680-2689; copy of abstract provided in **Exhibit M**), the first reports of transgenic goats were in 1991 (Ebert *et al.*, *Bio/Technology* **9**:835-838, and Denman *et al.*, *Bio/Technology* **9**:839-843; copies of abstracts provided in **Exhibit N**), and the first report of a transgenic monkey (rhesus monkey) was in January of 2001 (Chan *et al.*, *Science* **291**:309-312; copy of manuscript provided in **Exhibit O**). Additionally, the first report of a transgenic cow was in 1991 (Krimpenfort *et al.*, *Bio/Technology* **9**:844-847; copy of abstract provided in **Exhibit P**), the first report of a transgenic sheep (another example of a transgenic mammal) was in 1988 (Simons et al., *Bio/Technology* **6**:179-183; copy of abstract provided in **Exhibit Q**), and a report of the production of human anti-hemophilic factor IX in the milk of transgenic sheep was published in 1989 (Clark *et al.*, *Bio/Technology* **7**:487-492; copy of abstract provided in **Exhibit R**). Given the hundreds of reports of transgenic animals, of which the reports listed above are only the **first** examples, there can be no doubt that the making of transgenic animals is clearly enabled to those of skill in the art, which is all that is required to meet the enablement requirement under 35 U.S.C. § 112, first paragraph.

The Examiner further seems to believe that claims 8-9 are not enabled for transgenic animals because certain aspects of transgenic technology (expression levels, site-specific *versus* random integration) require some level of experimentation to perfect. However, Applicants respectfully point out that all that is required in order to satisfy the enablement requirement under 35 U.S.C. § 112, first paragraph, is making **any** transgenic animal, not the **perfect** transgenic animal. **Any** detectable level of expression of a transgene, for example SEQ ID NO:15, is all that is required, for it is well established that the enablement requirement is met if **any** use of the invention (or in this case, certain aspects of the

invention) is provided (*In re Nelson*, 126 USPQ 242 (CCPA 1960); *Cross v. Iizuka*, 224 USPQ 739 (Fed. Cir. 1985)). "The enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins Univ. v. CellPro, Inc.*, 47 USPQ2d 1705, 1719 (Fed. Cir. 1998), citing *Engel Indus., Inc. v. Lockformer Co.*, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991). Furthermore, a specification "need describe the invention only in such detail as to enable a person skilled in the most relevant art to make and use it." *In re Naquin*, 158 USPQ 317, 319 (CCPA 1968); emphasis added. Therefore, as the skilled artisan is clearly able to make a variety of different species of transgenic animals, claims directed at non-human transgenic animals are thus enabled and are supported by a specification that provides sufficient description to enable the skilled person to make and use the invention as claimed.

Therefore Applicants respectfully request the withdrawal of the present rejection, as the instant specification enables those of skill in the art to make and use the claimed invention.

III. Rejection of Claims 1-4 and 6-9 Under 35 U.S.C. § 112, Second Paragraph

The Action also rejects claims 1-4 and 6-9 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Action first rejects claims 1-4 for inclusion of Markush language which is no longer applicable to the present claims. Applicants have amended claims 1-4 to remove the offending language and thus this rejection has been avoided.

The Action further rejects claims 8-9 for allegedly being indefinite. Applicants respectfully traverse and submit that the term "host cell" is clearly defined and well known in the art and exemplified in the specification. Claims directed at a "host cell" have been allowed in hundreds of patents which indicates that it is clearly accepted as a definite term by the USPTO, since issued U.S. Patents are presumed to meet all of the requirements for patentability, including enablement under 35 U.S.C. §112, first and second paragraph. Therefore, Applicants respectfully submit that the presently claims directed at a host cell comprising the expression vector of Claim 4 must also, therefore, be enabled and sufficiently definite, and respectfully request withdrawal of this rejection.

Finally the Action rejects Claim 3 as being allegedly vague and indefinite due to a lack of a clear

definition of specific hybridization conditions. While Applicants submit that the claim as filed was sufficiently definite, as a number of stringent hybridization conditions are defined in the specification and would be known to those of skill in the art, solely in order to progress the case more rapidly toward allowance the claim has been revised to recite "hybrizes", a term which is clearly definite and well know to those of skill in the art. Applicants therefore submit that revised Claim 3 even more clearly meets the requirements of 35 U.S.C. § 112, second paragraph. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Based on the foregoing, Applicants submit that amended Claim 3 is sufficiently definite, and respectfully request withdrawal of this rejection.

IV. Rejection of Claim 1 Under 35 U.S.C. § 102(b)

The Action next rejects Claim 3 under 35 U.S.C. § 102(b), as being allegedly anticipated by Puschel, *et al.*, which describes a nucleotide sequence that is alleged to hybridize under stringent conditions to SEQ ID NO:15. Amended Claim 3 describes an isolated nucleic acid molecule comprising a nucleotide sequence that: (a) encodes the amino acid sequence shown in SEQ ID NO: 16; **and** (b) hybridizes to the nucleotide sequence of SEQ ID NO: 15 or the complement thereof. Thus, even if the sequences described in Puschel, *et al.*, could hybridize to SEQ ID NO:15, they would not encode the amino acid sequence shown in SEQ ID NO: 16 and thus do not properly anticipate all of the features of Claim 3. Applicants therefore respectfully request withdrawal of this rejection.

V. Rejection of Claim 1 Under 35 U.S.C. § 102(e)

The Action further rejects Claim 3 under 35 U.S.C. § 102(e), as being allegedly anticipated by Baker, *et al.*, which describes a nucleotide sequence that is alleged to hybridize under stringent conditions to SEQ ID NO:15. Amended Claim 3 describes an isolated nucleic acid molecule comprising a nucleotide sequence that: (a) encodes the amino acid sequence shown in SEQ ID NO: 16; **and** (b) hybridizes to the nucleotide sequence of SEQ ID NO: 15 or the complement thereof. Thus, even if the sequences described in Baker, *et al.*, could hybridize to SEQ ID NO:15, they would not encode the amino acid sequence shown in SEQ ID NO: 16 and thus Baker, *et al.* does not properly anticipate all of the features of Claim 3.

Applicants therefore respectfully request withdrawal of this rejection.

VI. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Gucker have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

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